EDITORIAL

Importance of concordance between left ventricular pacing sites and latest activated regions: myth or reality?

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Heart 2007;**93**:1170–1172. doi: 10.1136/hrt.2006.108837

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Cardiac resynchronisation therapy (CRT) is a well-established treatment in patients with severe and drug-refractory heart failure (New York Heart Association (NYHA) class III or IV) with severe left ventricular (LV) systolic dysfunction, dilated left ventricle and, lastly, LV dyssynchrony defined by a QRS duration ⩾120 ms on surface ECG.[1 2] In patients selected on the basis of these criteria, CRT significantly improves symptoms, exercise tolerance and quality of life and also reduces morbidity and mortality.[3–6] Despite a better comprehension of the physiopathology of cardiac dyssynchrony and technical improvements, especially in LV lead positioning in the tributary veins of the coronary sinus, a non-acceptable and stable rate of ''non-responders'' remains the Achilles' heel of CRT. However, the real rate of non-responders remains difficult to evaluate, particularly because of the heterogeneity of definitions of non-responders. In the MIRACLE trial, the rate of non-responders defined by a composite definition including death, worsening of heart failure or of global assessment and discontinuation of treatment and lack of improvement in NYHA class was 30%.[4] The rate of responders defined as patients alive with stable or improved NYHA class without increase in diuretic use in the latest published trial, the CARE-HF study, was 64%.[6 7] There are several reasons to explain the lack of efficacy of CRT in patients who are non-responders:

- An inappropriate or non-optimal selection of the patients on the basis of electrical criterion only (QRS width ⩾120 ms on 12-lead surface ECG) as a marker of cardiac dyssynchrony. Previous echocardiographic and magnetic resonance imaging studies have shown that there is not always a strong correlation between electrical and mechanical dyssynchronies, suggesting that patients with a wide QRS might not have mechanical dyssynchrony within the left ventricle and that by contrast a significant intra-LV dyssynchrony might be seen in patients with a ''narrow'' QRS (QRS width <120 ms).[8–11]
- The underlying cardiac disease and particularly the presence of an important myocardial scar without viability[12] or of an end-stage heart failure with severe right ventricular dysfunction and high pulmonary artery pressures might in some cases explain the lack of response to CRT.
- An inadequate programming of the CRT device. The programming of the device has to be tailored for each patient and especially atrioventricular and, perhaps or (probably?), interventricular delays. Classically, optimal paced and sensed atrioventricular delays are optimised using an echocardiographic measurement of the transmitral flow. These optimisations are time consuming and thus are not performed in all patients implanted with a CRT device.
- Finally, a non-optimal positioning of the ventricular leads—that is, left and right ventricular leads may explain the non-response to CRT. The ''classical'' optimal LV lead position is the lateral or posterolateral wall of the left ventricle.[13 14] The optimal location of the right ventricular lead has been not well established. The right ventricular lead is positioned either at the right ventricular apex or at the right ventricular septum.

In this issue of *Heart*, Becker *et al* report an elegant study to assess the impact of LV lead position on the efficacy of cardiac resynchronisation therapy using a two-dimensional strain echocardiography study (***see article on page 1197***).[15] Patients were divided into two groups according to the location of the LV lead and the site of the most delayed activation. Patients were defined as ''optimal'' as concurrence or immediate neighbouring of the segment with the latest contraction before CRT, and those with assumed LV location defined as the site with the maximal temporal difference in peak circumferential strain (ie, with the greatest reduction in contraction delay due to CRT). The efficacy of CRT was compared between the two groups, optimal LV lead placement and non-optimal LV lead placement, using a composite end point including the absence of admission to hospital for heart failure and improvement in NYHA class, or if NYHA was unchanged a >10% increase in peak oxygen consumption, $V_{O_2}max$, with a short follow-up time of 3 months. Patients with an optimal LV lead placement had a non-responder rate of 4% and patients without an optimal LV lead placement a non-responder rate of 22%. Interestingly, the magnitude of improvement in the LV ejection fraction and in $V_{O_2}max$ decreased with increasing distance of the assumed LV lead location from the segment with the latest mechanical contraction at baseline.

Abbreviations: CRT, cardiac resynchronisation therapy; LV, left ventricular; NYHA, New York Heart Association

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Previous studies suggested that the magnitude of LV dyssynchrony assessed by conventional or tissue Doppler imaging echocardiographic techniques was a stronger predictor of response to CRT than baseline QRS duration.[16] The predictive value of the reduction in QRS width with CRT is controversial.[16] We demonstrated that in responder patients the QRS duration was reduced by 37 ms and by only 11 ms in non-responder patients. During the implantation after the LV lead implantation in the lateral or posterolateral LV wall, the position of the right ventricular lead was optimised to provide the narrowest QRS duration with a normal axis. In our experience, in most of cases the right ventricular lead was screwed in the mid-septum.[17] The location of the LV pacing lead is certainly of major importance, but LV lead implantation remains highly dependent on the anatomy of the coronary sinus (distribution of collateral veins) and technical issues such as pacing and sensing thresholds and the absence of phrenic nerve stimulation.

The importance of the knowledge of the site of latest activation and its concordance with the LV pacing site has already been demonstrated.[18–20] Using pulsed-wave tissue Doppler imaging, Ansalone *et al* showed that patients paced at the site of greatest delay had a more favourable response in LV ejection fraction, LV end-systolic volume and exercise load.[18] Using a tissue synchronisation imaging technique, Murphy *et al* demonstrated in 54 patients that a concordant LV pacing site with the most delayed activated site yielded a significant improvement in NYHA class and LV reverse remodelling as compared with discordant pacing sites.[19] The importance of the concordance of the LV pacing site and the most delayed segment assessed by two-dimensional strain has also been demonstrated by Suffoletto *et al*, who achieved a significantly higher magnitude of improvement in the LV ejection fraction in patients with concordant LV lead position.[20]

Another important finding of Ansalone's study was that in 43% of patients the site of the latest activation was not a lateral or posterolateral segment, suggesting the importance of the identification of the latest activation site before CRT implantation.[18] In the present study, 32% of the most delayed segments were anterior and inferior.[15] These data suggest that a systematic lateral or posterolateral position of the LV lead would not be appropriate in all patients selected for CRT and thus should be tailored to suit each patient.

Becker *et al* performed an echocardiographic study using a new sophisticated echocardiographic technique with an evaluation of the circumferential strain to assess cardiac dyssynchrony.[15] Many echocardiographic techniques are currently available for evaluating LV dyssynchrony.[21] Among the most recent techniques, the two-dimensional strain or speckle tracking seems promising because it calculates myocardial strain independently of angle of incidence.[20] A previous study assessed the accuracy of longitudinal or radial strain to evaluate cardiac dyssynchrony.[20 22 23] In the present study, the authors evaluated the circumferential strain.[15] Conceptually, measurement of the strain (regional active deformation) appears more ''appropriate'' than evaluation of the myocardial velocity that may reflect passive as well as active motion. A myocardial velocity may be passive owing to tethering or translation of the entire heart. For example, the basal regions may have longitudinal velocity after myocardial infarction, if the mid-ventricular segments contract normally. However, analysis of strain after processing might be limited by signal to noise ratio and is not available in all echocardiography. Usually, to evaluate the cardiac dyssynchrony with the strain analysis, only the time to the peak of the strain is considered but not the magnitude of the strain. This might be a limitation of the technique because a low strain amplitude below 5% remains highly questionable. A major concern with all the echocardiographic studies is the lack of evidence. Most of the studies were conducted in a small group of patients and only in one or two centres, and without core-laboratory analysis. Only one multicentre study designed to assess prospectively the echocardiographic variables has been completed, the PROSPECT trial, and results should be available at the end of this year.[24]

In conclusion, identification of the latest mechanical sites before implantation of CRT devices remains an important step in each patient to define the optimal LV pacing site. However, if LV lead positioning is important, the location of the right ventricular lead has also to be optimised to improve the efficacy of CRT. What can we expect for improving the positioning of the leads? A per-operative evaluation of cardiac dyssynchrony with echocardiographic measures to guide the right and LV leads? This solution seems very attractive but not really feasible in daily practice in all centres. Another solution might be a pre-operative evaluation of cardiac dyssynchrony using different techniques (echocardiography, magnetic resonance imaging, electrical mapping and coronary sinus anatomy (CT, coronary sinus angiography) with data fusion and simulation of the combination of different pacing sites.

Conflict of interest: None declared.

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IMAGES IN CARDIOLOGY

doi: 10.1136/hrt.2006.104125

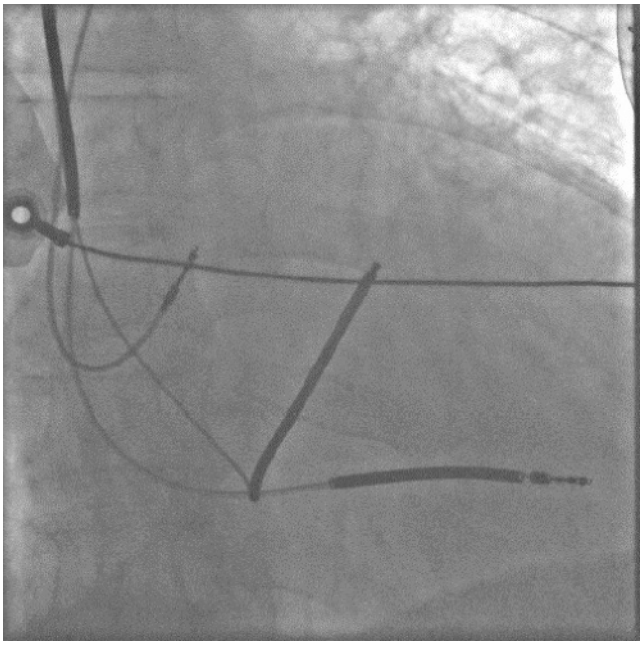
Additional coronary sinus shocking lead improved defibrillation threshold

A 61-year-old man was referred for treatment of recurrent syncopal ventricular arrhythmias, including two documented episodes of ventricular fibrillation (VF) due to alcohol-induced dilated cardiomyopathy. The patient had been taking amiodarone for 8 months. In addition he was taking an ACE inhibitor and spironolactone. A standard 12-lead ECG showed normal sinus rhythm with a QRS duration of 118 ms. Echocardiography confirmed the presence of severely impaired left ventricular function with an ejection fraction of <20%.

A dual-chamber, high-output ICD device (St Jude Medical, AtlasTM +DR, 46 J stored; 36 J delivered) using a transvenous defibrillation lead with distal RV apex coil (anode) and a proximal SVC coil (cathode) was implanted. VF was induced by 50 Hz burst pacing. The device delivered 36 J shocks, which failed to restore sinus rhythm, and external cardioversion was required. Despite reversal of shocking polarity, disconnecting the SVC coil and manipulation of the shock wave form, the defibrillation threshold (DFT) remained unacceptably high (>30 J). The possibility of a high DFT due to amiodarone treatment was considered and amiodarone was replaced with sotalol, which has been shown to improve DFT.

The patient underwent repeat DFT testing 1 month later. VF was induced with 50 Hz burst pacing and the device delivered a 36 J shock, which again failed to restore sinus rhythm. We subsequently positioned a Medtronic-TRANSVENE-SVC lead in the coronary sinus by shaping a stylet to facilitate introduction (see panel). The SVC coil was capped. Repeat testing showed a dramatic reduction in DFT with successful cardioversion on two consecutive occasions at 18 J.

This case demonstrates the benefit of an additional left-sided shocking lead in decreasing the DFT. This is a less invasive procedure than a subcutaneous array or an epicardial patch. Studies to look for alternative locations for defibrillator electrodes showed successful defibrillation with electrodes placed in the coronary sinus. However, in these studies, patients with conventional right-sided defibrillators had DFTs within the accepted normal range, whereas our patient had an unacceptably high DFT with the initial implantation. In conclusion, the addition of a left-sided shocking coil lead may achieve a marked reduction in defibrillation threshold.



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